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Familial Melanoma Aggregation in North-Eastern Italy

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To the Editor:

The incidence of cutaneous melanoma (CM) in Caucasians has been growing at a rate of 3%−7% per year since the early 1960s. It has doubled in the last 20 y, and is increasing faster than any other cancer (Armstrong & English, 1996; Ferlay *et al.* 1996). In 1990 the CM Italian crude incidence rate was approximately 7.6 cases per 100,000 per year (World standard population rate of 3.6 for men and 4.1 for women) (Balzi *et al.* 1997).

Approximately 6%−18% of CM patients has at least one first-degree relative with melanoma (Greene & Fraumeni, 1979; Goldstein & Tucker, 1995).

The proportion of familial cases among population-based patients has rarely been studied in Italy. Between January 1994 and December 1999, 589 consecutive incident patients (264 men, 325 women, mean age 53.2, range 17-88) were diagnosed and surgically treated for primary CM at the Dermatology Unit of the M. Bufalini Hospital, Cesena, Italy.

The Dermatology Unit is a reference point for the regions of Southern Emilia-Romagna and Northern Marche, located between 43°, 50' and 44°, 10' parallel North, with a population of around 1,000,000. The patients referred to the clinic are representative of the entire area. The Bufalini Hospital Ethical Committee approved the study and informed consent was obtained on all participants. During hospitalization, the 589 incident CM patients were interviewed about the occurence of melanoma in their relatives. Pathologic reports and slides of the tumors of the patients' relatives were required to confirm the diagnosis.

Thirty subjects (5.1%) reported that at least one of their relatives had CM.

Pathology reports were obtained for 28 of the 30 patients thought to have CM (93.3%). In the remaining two cases, histologic confirmation could not be obtained because the relatives had died 30 or more years before. Slide reviews revealed 28.6% (eight subjects) false reports: for five patients, the reported CM was actually a melanocytic nevus, for two relatives, a basal cell carcinoma and for one, an actinic keratosis. Thus, 20 of 589 patients (3.4%) had a relative with a confirmed CM. Among them, cases were first-degree relatives in 15 families (2.5%), second-

degree relatives in two families (0.3%), and third-degree relatives in three families (0.5%). The phenotypic and clinical characteristics of these families have been described elsewhere (Landi *et al.* 1999).

Previous reports of a family history of CM varied depending on the geographical area. The incidence of CM is substantially higher among fair-skinned people, and familial aggregation reflects or contributes to the high risk. Also, population differences in age, family size, and environmental factors may affect familial aggregation. In Holman & Armstrong 1984) found a positive family history in 15% of 507 cases (9.9% in first-degree relatives) and Green *et al.* (1985) in 18% of 183 cases (9.5% in first-degree relatives). In Italy, Cristofolini and colleagues (Cristofolini *et al.* 1987) found four subjects out of 103 cases (3.9%) with CM in first-degree relatives. Similarly, in the U.S.A., first-degree relatives with CM were present in 4.1% of 116 CM cases (Holly *et al.* 1987). In Denmark, among 474 patients, 4.7% had a blood relative with CM (3.0% in first-degree relatives) (Østerlind *et al.* 1988). For the above studies, specific information on first-degree relatives was presented by Ford *et al.* ; all these data, however, lacked histologic confirmation (Ford *et al.* 1995).

Additional studies have examined the accuracy of self-reported family history. In a cohort of 276 consecutive American CM patients, melanoma in relatives was histologically confirmed in 27 of the 31 subjects (87%) who had initially reported a family history for CM.[1] In an Australian study, Aitken *et al.* showed that about 40% of self-reported melanomas in familial settings were incorrect. In that study, people affected by CM tended to over-report melanoma in their family members compared with other cancers involving the breast, colon, and pancreas (Aitken *et al.* 1996).

In this study, 2.5% of 589 CM patients had a confirmed family history of melanoma in first-degree relatives. Overall, familial CM represents a small fraction of the melanoma burden. If we consider the emerging increase in the melanoma incidence rate in western countries, however, the prevalence of familial melanoma clustering is becoming considerable. The identification of genes, host, and environmental factors involved in these aggregations may help to elucidate the etiology of both familial and sporadic CM, and have a significant impact on prevention and clinical activities.

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